Prevalence of intestinal complications in inflammatory bowel disease: a comparison between paediatric-onset and adult-onset patients

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Abstract: INTRODUCTION: Intestinal complications in inflammatory bowel disease indicate active inflammation and typically result in the intensification of therapy. AIM: To analyse whether the rates of intestinal complications were associated with age at disease onset. PATIENTS AND METHODS: Data from 1506 individuals with Crohn's disease (CD) and 1201 individuals with ulcerative colitis (UC) were obtained from the Swiss inflammatory bowel disease cohort study database, classified into groups on the basis of age at diagnosis (<10, <17, <40 and >40 years of age), and retrospectively analysed. RESULTS: In CD patients, the rates of stricturing (29.1-36.2%), abdominal penetrating disease (11.9-18.2%), resectional surgery (17.9-29.8%) and perianal disease (14.7-34.0%) were correlated with disease duration, but not age at diagnosis. However, paediatric-onset CD was associated with higher rates of multiple, rectal and anal strictures and earlier colon surgery. In addition, perianal disease occurred earlier, required earlier surgical intervention, and was more often combined with stricturing and penetrating disease. Finally, anal fissures were more prevalent among younger patients. In UC patients, the rates of progression or extension of disease (0-25.8%) and colectomy (3.0-8.7%) were dependent on disease duration, but not age at disease onset. Paediatric-onset disease was associated with a higher rate of extensive colitis at diagnosis and earlier progression or extension of disease, and nonsurgically treated patients with the youngest ages at onset more frequently required antitumour necrosis factor- treatments. CONCLUSION: The higher rates of intestinal complications, including those of the small and large bowel and in the anal region, in paediatric-onset CD patients point towards a level of inflammation that is more difficult to control. Similar findings were also evident in UC patients.

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Prevalence of intestinal complications in inflammatory bowel disease: a comparison between paediatric-onset and adult-onset patients

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Introduction Intestinal complications in inflammatory bowel disease indicate active inflammation and typically result in the intensification of therapy.
Aim To analyse whether the rates of intestinal complications were associated with age at disease onset.
Patients and methods Data from 1506 individuals with Crohn's disease (CD) and 1201 individuals with ulcerative colitis (UC) were obtained from the Swiss inflammatory bowel disease cohort study database, classified into groups on the basis of age at diagnosis (< 10, < 17, < 40 and > 40 years of age), and retrospectively analysed.
Results In CD patients, the rates of stricturing (29.1–36.2%), abdominal penetrating disease (11.9–18.2%), resectional surgery (17.9–29.8%) and perianal disease (14.7–34.0%) were correlated with disease duration, but not age at diagnosis. However, paediatric-onset CD was associated with higher rates of multiple, rectal and anal strictures and earlier colon surgery. In addition, perianal disease occurred earlier, required earlier surgical intervention, and was more often combined with stricturing and penetrating disease. Finally, anal fissures were more prevalent among younger patients. In UC patients, the rates of progression or extension of disease (0–25.8%) and colectomy (3.0–8.7%) were dependent on disease duration, but not age at disease onset. Paediatric-onset disease was associated with a higher rate of extensive colitis at diagnosis and earlier progression or extension of disease, and nonsurgically treated patients with the youngest ages at onset more frequently required antitumour necrosis factor-α treatments.
Conclusion The higher rates of intestinal complications, including those of the small and large bowel and in the anal region, in paediatric-onset CD patients point towards a level of inflammation that is more difficult to control. Similar findings were also evident in UC patients. Eur J Gastroenterol Hepatol 29:926–931

Introduction

Intestinal complications developing during the course of inflammatory bowel disease (IBD) indicate active inflammation and disease progression or extension, typically resulting in the intensification of medical therapy or in s urgical intervention. Intestinal complications, including stricture, abscess and fistula development, are present in 38% of patients within the first 10 years of paediatric-onset Crohn's disease (CD) [1] and in 31.6% of patients with adult-onset CD [2]. Previous studies have also shown that patients with CD diagnosed before the age of 40 years have more disabling disease outcomes [3] and that disease progression or extension is more rapid in childhood-onset IBD [4]. Data suggest that within 10 years after being diagnosed with ulcerative colitis (UC), 14% of adult-onset patients will have experienced progression or extension of disease [5], whereas 50% of paediatric-onset patients will experience a similar outcome [6,7]. In contrast, the colectomy rate has been reported to be similar in both age groups, namely, 20% in patients with paediatric onset after the age of 5 years [6–8] and 8.7–28% in adult-onset patients with UC [5].

Little is known about the prevalence of intestinal complications in paediatric or adult patients in Switzerland after stratification by age at disease onset. In 2006, the Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS), a nationwide cohort study on patients with IBD, was initiated [9]. The aim of the present study was to assess the prevalence of intestinal complications in this study cohort and stratify patients according to age at disease onset. We hypothesized that disease onset during childhood would be a risk factor for a higher complication rate.

Patients and methods

As of March 2014, 2972 patients diagnosed with CD, UC or inflammatory bowel disease-unclassified (IBD-U) according to standard criteria [9] were registered in the SIBDCS database. The study protocol for this cohort study was approved by the

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central and local ethics committees in Switzerland in 2006. Patient recruitment was performed at the following six university centres in western and eastern Switzerland, Geneva, Lausanne, Bern, Basel, Zurich and St Gallen, as well in selected regional centres, with the University of Lausanne serving as the coordinating centre and housing the database [10]. Retrospective data since diagnosis were obtained from patient charts, and clinical data were collected during medical visits at inclusion and follow-up by the patient's gastroenterologist or a specialized study nurse who completed clinical report forms. The forms were then sent to the data centre for validation and data entry. The following data were obtained from this database: date of birth, sex, family history of IBD (first degree relatives), age at IBD diagnosis and at inclusion, type of IBD (CD, UC, IBD-U), disease location (recorded according to Montreal classification) [11] on the basis of the endoscopies, radiological assesements or surgical interventions, and comprehensive histological results (epithelioid granulomas, chronic architectural changes or mucosal secretion depletion). Furthermore, data on the occurrence of strictures (duodenojejunal, ileal, ileocaecal valve, colon, rectum and anus, and anastomosis, as diagnosed by endoscopic, radiologic or surgical means), abdominal penetrating disease (enteroenteral, enterovesical, enterocutaneous fistulas and perforation and intra-abdominal abscesses as diagnosed by radiologic or surgical means), perianal disease (PD) (high and low perianal, perineal, vaginal fistulas, chronic or acute anal fissures and perianal abscesses as diagnosed by clinical, radiologic or surgical examination) in CD and progression or extension of disease and ileal involvement in UC were retrieved. In addition, data on the necessity of treatments that were considered to indicate disease progression, such as the need for tumour necrosis factor-α inhibitors (anti-TNF-α), independent of success, failure or cessation for adverse effects, and the necessity for abdominal resectional surgery [small bowel, ileocaecal or any type of colonic resection (right, left, sigmoid resection, subtotal colectomy or total proctocolectomy)] or perianal surgery (abscess drainage, fistulectomy, seton placement, fibrin/glue instillation and mucosal sliding flap) were obtained. The outcome was defined as the presence of stricturing, penetrating or PD in CD, progression or extension of disease or backwash ileitis in UC, or need for therapies such as surgery or anti-TNF-α therapy. The patients were grouped according to the Paris classification [12] into categories on the basis of age at diagnosis (<10, <17 and $<$ or >40 years). The outcome variables were dichotomized into present or absent.

Statistics

The distribution of continuous data was assessed using Normal-QQ-plots. Gaussian distributed data are presented as the mean ± SD and range, and non-Gaussian distributed data are presented as the median and interquartile range. Differences in the distribution of continuous data between the two groups were assessed using Student's *t*-test for Gaussian data or the Wilcoxon–Mann–Whitney rank sum test for non-Gaussian data. Differences in continuous data distribution between more than two groups were assessed using Fisher's *F*-test for Gaussian data or the Kruskal–Wallis test for non-Gaussian data. Categorical data are presented as raw counts and relative percentages. Differences in the distribution of categorical data between the groups were assessed using the χ^2-test or Fisher's exact test in cases of insufficient sample size. Bonferroni's correction was used for multiple testing. Kaplan–Meier estimates were used to assess the complication-free survival time during SIBDCS follow-up and the log-rank test was used to assess differences between survival curves. Multivariate Cox proportional hazard regression was used to estimate the rates of complication-free survival in association with variables with unknown intervals between disease onset and the occurrence of the complication before study inclusion. Logistic regression was used to assess associations between complications and age categories after adjustment for disease duration. For the purpose of the present study, a *P*-value of less than 0.05 was considered statistically significant. Statistical analyses were carried out using SPSS statistics 23.0 (IBM, Armonk, New York, USA).

Results

After the exclusion of 76 patients with IBD-U, 155 patients with CD and 34 patients with UC because of incomplete data, data for 1506 (718 male, 888 female patients) patients with CD and 1201 (642 male, 559 female patients) patients with UC were analysed.

Patients with Crohn's disease

For a description of the baseline characteristics, see Table 1. Only a few patients had an additional assessment of the upper gastrointestinal tract performed after diagnosis with CD (13/47 patients the <10 years age class, 42/182 patients in the <17 age class, 125/1000 patients in the <40 age class and 41/277 patients in the >40 years age class); thus, this location of initial assessment was not included with the analysis. No sex difference was identified between age groups; therefore, we analysed male and female patients together.

The comparisons of the rate of intestinal complications between age groups yielded the following results:

The overall prevalence of strictures was the same in all age groups, but when looking at specific stricture types, the rate of rectal and anal strictures was higher in patients with the youngest age at onset. Furthermore, multiple strictures were more frequent in paediatric-onset patients (Table 1). The results of the survival analysis by age group showed no difference in the intervals between disease onset and the occurrence of colonic (log-rank $P=0.17$) or small bowel strictures (log-rank $P=0.29$). Looking at the adult-onset cohort separately, strictures overall (Pearson's $\chi^2=45.4$, $P<0.001$) and small bowel (Pearson's $\chi^2=85.6$, $P<0.001$) or colonic strictures (Pearson's $\chi^2=10.1$, $P=0.04$) specifically were correlated with the initial location and with the presence of granulomas (Pearson's $\chi^2=19.6$, $P<0.001$) at diagnostic biopsy. In contrast, in the paediatric-onset group, no such correlation was found.

Overall, abdominal penetrating disease occurred at a similar rate in patients of all age categories (Table 1), and the rates were also similar when fistula types were analysed individually (enteroenteral: 28.6–45.5%, $P=0.9$; enterovesical: 12.1–28.6% $P=0.7$; enterocutaneous: 25.8–33.3% $P=0.8$). The duration from CD diagnosis to the manifestation of penetrating disease was similar in all age classes (log-rank $P=0.4$). Only the rate of intra-abdominal abscesses was correlated with younger age at disease onset

Table 1. Characteristics and disease behaviour of patients with Crohn's disease

	Age category [*n* (%)] (years)				
	< 10 (*n* = 47)	< 17 (*n* = 182)	< 40 (*n* = 1000)	> 40 (*n* = 277)	*P*[a]
Sex (male) (%)	29 (61.7)	101 (55.5)	452 (45.2)	136 (49.0)	NS
Age at diagnosis [median (IQR)] (months)	90 (61)	163.5 (34)	295.0 (121)	619 (175)	
Positive family history	12 (25.5)	29 (15.9)	134 (13.4)	32 (11.5)	0.5
NA	2 (4.3)	14 (7.7)	73 (7.3)	21 (7.5)	
Initial location					
L1	6 (12.8)	22 (12.1)*	248 (24.8)*	89 (32.1)*	< 0.001*
L2	11 (23.4)	28 (15.4)*	216 (21.6)	83 (30.0)*	0.01*
L3	29 (61.7)[&]	128 (70.3)*	233 (23.4)*,[&]	37 (13.4)*,[&]	0.001*,[&]
L4	1 (2.1)	4 (2.2)	8 (0.8)	3 (1.1)	
Histology at diagnostic biopsy					
Granuloma	23 (50.0)*	64 (35.6)[&]	233 (23.4)*,[&]	37 (13.4)*,[&]	0.006*,[&]
NA	2 (4.3)	22 (12.2)	155 (15.6)	47 (17.0)	
Disease duration up to last FU [median (IQR)] (months)	82.5 (143)	67.5 (149)*	133.0 (171)*	88.0 (107)	0.02*
All strictures (SD)	17 (36.2)	53 (29.1)	391 (39.2)	93 (33.3)	NS
Multiple strictures, excluding anastomotic	5 (29.4)*	10 (18.9)[&]	28 (7.2)*,[&]	5 (5.4)*	0.02*,[&]
Duodenojejunal	3 (17.7)*	4 (7.6)	13 (3.3)*	3 (3.2)	0.02*
Ileal	10 (58.8)	32 (60.4)	240 (61.4)	66 (71.0)	0.3
Colonic	4 (23.5)	14 (26.4)	85 (21.7)	15 (16.1)	0.4
Rectal	3 (17.7)	0	16 (4.1)*	1 (1.1)*	0.01*
Anal	3 (17.7)*	4 (7.5)	18 (4.6)	1 (1.1)*	0.01*
Total PND	7 (14.9)	33 (18.1)	182 (18.2)	33 (11.9)	NS
Enteroenteral, enterovesical, enterocutaneous	6 (85.7)	27 (81.8)	146 (87.9)	30 (90.9)	NS
Intra-abdominal abscess	2 (28.6)	17 (51.5)	88 (48.4)	8 (24.2)	NS
Total PND and SD	7 (14.9)	19 (10.4)	115 (11.5)	18 (6.5)	NS
Total resectional surgery, single or multiple	14 (29.8)	26 (14.3)	230 (23.0)	50 (17.9)	NS
Resectional surgery and anti-TNF-α	8 (57.1)	9(34.6)	84 (36.5)	16 (32.0)	NS
Anti-TNF-α, no surgical intervention	13 (27.7)	43 (23.6)	290 (29.0)	61 (22.0)	NS

L1, ileal; L2, colonic; L3, lleocolonic.; L4, upper gastrointestinal tract.
FU, follow-up; IQR, interquartile range; PND, abdominal penetrating disease; SD, stricturing disease; TNF-α, tumour necrosis factor-α.
[a]Bonferroni corrected differences.
*variables with significant difference.

(Pearson's $\chi^2 = 12.5$, $P = 0.006$). In the adult-onset group alone, no correlations between the rate of penetrating disease and initial location or the presence of granuloma at diagnosis were identified. In the paediatric cohort, only the presence of granulomas at initial biopsy was correlated with the rate of penetrating disease (Pearson's $\chi^2 = 11.2$, $P = 0.004$).

The rate of resectional surgery for stricturing or penetrating disease was the lowest in patients with disease onset less than 17 years. The survival analysis by age group showed that colonic resectional surgery occurred significantly earlier in patients with disease onset before the age of 10 years (log-rank $P = 0.048$), whereas the intervals between disease onset and small bowel (log-rank $P = 0.5$) and ileocaecal resectional surgery (log-rank $P = 0.132$) were similar in all age groups.

The overall rate of perianal fistulizing disease (PD) (Table 2) and the rates of individual fistula types [low (32.8–34.8%, $P = 0.7$), high (3.5–8.7%, $P = 0.6$), perineal (11.5–22.5% $P = 0.2$) or vaginal fistula (4.3–12.9%, $P = 0.5$)] were similar in all age groups. The rate of fistulizing PD was correlated with the rate of stricturing disease (Pearson's $\chi^2 = 7.9$, $P = 0.005$), but not with that of penetrating disease, initial location or granulomas in the paediatric cohort. In contrast, in adult-onset patients, the rate of fistulizing PD was correlated with stricturing (Pearson's $\chi^2 = 11.6$, $P = 0.001$), penetrating disease (Pearson's $\chi^2 = 22.5$, $P < 0.001$), initial disease location (Pearson's $\chi^2 = 30.0$, $P < 0.001$) and granuloma at initial biopsy (Pearson's $\chi^2 = 9.7$, $P = 0.01$). Anal fissures were significantly more prevalent in the patients with the youngest age at onset, but no correlation was identified between anal fissures and any of the other variables tested. In adult-onset patients, anal fissures were correlated with colonic initial disease location (Pearson's $\chi^2 = 12.8$, $P = 0.01$).

The rates of the assessed treatments (anti-TNF-α antibodies or surgical intervention) were similar in paediatric and adult disease onset CD. The results of the survival analysis, however, showed that PD (log-rank $P = 0.022$) and perianal surgery (log-rank 0.006) occurred significantly earlier in paediatric-onset than adult-onset CD patients.

The results of the multivariate Cox proportional hazard regression did not show any associations between age at disease onset and the development of colonic or small bowel stricturing disease, abdominal penetrating disease or PD (Table 3) or the requirement of surgical intervention. Only having required anti-TNF-α therapy was identified as a risk factor for penetrating disease and surgery of the colon [relative risk (RR): 1.2; 95% confidence interval (CI): 1.04–1.37; $P = 0.02$], small bowel (RR: 1.2; 95% CI 1.01–1.40; $P = 0.04$) or perianal region (RR: 1.2%; 95 CI: 1.03–1.38; $P = 0.02$), independent of the age at diagnosis of CD.

Patients with ulcerative colitis

For a description of the baseline characteristics, see Table 4. The sex distributions between age groups and the variables tested were similar; therefore, male and female patients were analysed together. The comparisons of the rate of complications between age groups yielded the following picture:

Progression or extension of disease (Table 4) occurred at a similar rate in all age classes, but the results of the survival analysis showed that this complication occurred

Table 2. Perianal disease and treatments at any time after diagnosis

	Age category [*n* (%)] (years)				
	< 10 (*n* = 47)	< 17 (*n* = 182)	< 40 (*n* = 1000)	> 40 (*n* = 277)	*P*[a]
Total fistulizing PD, patients	16 (34.0)*	42 (23.1)	268 (26.9)*	41 (14.7)*	0.006*
Perianal abscess, patients	8 (50.0)	24 (68.6)	126 (47.0)	20 (48.8)	0.7
Low, high, perianal, perineal or rectovaginal fistula	14 (87.5)	30 (57.1)	223 (83.2)	34 (82.9)	0.3
Anal fissure	11 (23.4)*	19 (10.4)	81 (8.1)*	22 (7.9)*	0.006*
SD and/or PND	7 (77.8)	18 (62.1)	161 (57.9)	23 (54.4)	0.6
Surgical intervention, patients	13 (81.3)	35 (83.3)	200 (74.6)	30 (73.2)	0.6
Surgical intervention and anti-TNF-α	8 (34.8)	14 (26.9)	98 (30.2)	10 (17.2)	0.21
Anti-TNF-α, no surgical intervention	5 (21.7)	11 (21.2)	74 (22.8)	15 (25.9)	0.9

PD, perianal disease; PND, penetrating disease; SD, stricturing disease; TNF-α, tumour necrosis factor-α.
[a]After Bonferroni correction.
*variables with significant difference.

Table 3. Association between age at disease onset, initial disease location or having ever been treated with anti-TNFα and outcome in patients with CD (Multivariate Cox proportional hazard regression)

	Small bowel stricture			Colonic stricture			Abdominal penetrating disease			Perianal disease		
Outcome	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*
Disease onset < 17 years	0.62	[0.36–1.18]	0.15	0.37	[0.16–0.86]	0.02	1.16	[0.51–2.64]	0.72	0.55	[0.33–0.91]	0.02
Disease onset < 40 years	0.75	[0.42–1.32]	0.32	0.43	[0.22–0.85]	0.02	0.97	[0.45–2.07]	0.94	0.54	[0.35–0.84]	0.01
Disease onset > 40 years	0.93	[0.51–1.70]	0.80	0.36	[0.16–0.81]	0.01	0.92	[0.41–2.09]	0.85	0.53	[0.32–0.87]	0.01
L1	1.07	[0.43–2.64]	0.88	NA*			0.73	[0.23–2.34]	0.59	2.72	[0.38–19.75]	0.32
L2	0.17	[0.07–0.44]	< 0.001	NA*			0.51	[0.16–1.64]	0.26	4.81	[0.67–34.77]	0.12
L3	0.70	[0.29–1.71]	0.43	NA*			0.72	[0.23–2.28]	0.58	4.46	[0.62–32.22]	0.14
Ever treated with anti-TNFα	1.01	[0.86–1.19]	0.91	1.12	[0.91–1.39]	0.29	1.16	[1.01–1.34]	0.04	1.1	[0.97–1.241]	0.12

Age category < 10 years and upper GI initial location are treated as base risk, and do not appear.
L1, ileal; L2, colonic; L3, Ileo-colonic.
*Not possible to evaluate: too few cases.

earlier in paediatric-onset patients (log-rank $P = 0.03$). In the adult cohort, disease progression was correlated with ileal involvement (Pearson's $\chi^2 = 140.4$, $P < 0.001$), but not with mucosal secretion depletion or chronic architectural changes at initial biopsy or the need for colonic resection. In the paediatric-onset cohort, progression or extension of disease was not correlated with any variables. Backwash ileitis occurred at a similar rate in all age groups, but later (log-rank $P = 0.002$ for age group < 10 years) in the youngest-onset group. The rate of colectomy did not differ between age groups and occurred within the same interval from diagnosis in all age groups (log-rank $P = 0.678$). The rate of treatments with anti-TNF-α antibodies was higher in paediatric-onset patients without colectomy (Table 4).

The results of the multivariate Cox proportional hazard regression showed that age at diagnosis was not a risk factor for any of the assessed complications; that left-sided colitis, independent of age at diagnosis, was associated with disease extension; and that age older than 40 years was associated with backwash ileitis and anti-TNF-α treatments (Table 5).

Discussion

The investigation of whether the rates and types of intestinal complications were dependent on the age at disease onset yielded the following results: at baseline, our CD age groups [12] differed significantly in terms of initial disease location, histological markers at diagnostic biopsy and disease duration, differences that have been reported previously by other studies [4,13–18]. Thus, we compared unequal groups for the development of intestinal complications. Despite these differences, the overall prevalence rates of strictures (29–39%) and of penetrating abdominal disease (11.9–18.2%) were similar in all age groups and dependent on disease duration, but not age at disease onset, which was consistent with former reports [3,4, 13–16]. Furthermore, stricture location, at least in adult-onset patients, reflected initial disease location as described previously [19,20]. In addition, perianal fistulizing disease occurred at a similar rate in all age classes (14.7–34.0%) and at rates comparable with previous reports [4,15].

However, we found that the rates of multiple strictures, especially small bowel strictures, were significantly higher in paediatric-onset patients, the rate of rectal and anal strictures was the highest in the CD patients with the youngest age at onset and that the location of strictures was not correlated with initial disease location as reported previously in adult-onset patients [19,20]. Second, even though the need for resectional surgery was much lower in pubertal-onset patients, colonic surgery was carried out earlier during the course of disease in the patients with the youngest age at onset as described by other studies [19–22]. Third, when looking at PD, we found any type of PD and surgical intervention to occur significantly earlier in CD patients with the youngest age at onset. In addition, perianal fistulizing disease was more prevalent among patients with stenosing or penetrating disease, but not correlated with initial disease location, as reported in adult patients [13,23,24]. Finally, anal fissures (47.8 and 34.6%) were significantly more prevalent in paediatric-onset CD, and the rate was much higher than that reported by a recent study [25].

Table 4. Patient characteristics of patients with ulcerative colitis according to age at diagnosis

	Age category [*n* (%)] (years)				
	< 10 (*n* = 42)	< 17 (*n* = 99)	< 40 (*n* = 771)	> 40 (*n* = 289)	*P*[a]
Sex (male) (%)	17 (40.5)	47 (47.5)	397 (51.5)*	181 (62.6)*	0.006*
Age at diagnosis [median (IQR)] (months)	84 (62)	161 (33)	328 (131)	615 (167)	
Positive family history	5 (11.9)	13 (13.1)	86 (11.2)	23 (8.0)	0.2
NA	0	11 (11.1)	65 (8.5)	32 (11.1)	
Initial location					
E3	33 (78.6)*	64 (64.7)[&]	323 (41.9)*,[&]	104 (36.0)*,[&]	< 0.001*,[&]
E2	5 (11.9)*	16 (16.2)*	258 (33.5)*	115 (39.8)*	0.02
E1	2 (4.7)	14 (14.1)	157 (20.4)	59 (20.4)	NS
NA	2 (4.7)	5 (5.1)	65 (8.4)	20 (6.9)	0.7
Histology at diagnostic biopsy					
Mucosal secretion depletion	12 (30.0)	23 (25.3)	156 (22.4)	75 (27.9)	0.2
Chronic architectural changes	29 (72.5)*	50 (54.9)	304 (43.7)*	147 (54.6)	< 0.001*
NA	0	4 (4.4)	91 (13.1)	27 (10.0)	
Positive family history	5 (11.9)	13 (13.1)	86 (11.2)	23 (8.0)	0.2
NA	0	11 (11.1)	65 (8.5)	32 (11.1)	
Disease duration up to last FU [median (IQR)] (months)	82.5 (143)*	67.5 (149)*	133 (171)*	88 (107)	< 0.001*
Progression of disease extension					
Progression (E1 + E2)	2 (28.6)	9 (30.0)	109 (26.3)	34 (19.5)	0.3
Endoscopy after inclusion	7 (16.7)*	19 (19.2)	217 (28.2)	101 (35.0)*	0.02*
Ileal involvement	2 (4.8)	10 (10.1)	141 (18.3)	57 (19.7)	NS
Massive haemorrhage	1 (2.4)	4 (4.0)	19 (2.5)	3 (1.0)	0.3
Perforation	0	0	5 (0.7)	3 (1.0)	0.6
Colonic resection	4 (9.5)	4 (4.0)	92 (11.9)	30 (10.4)	0.1
Total colectomy	3 (7.1)	3 (3.0)	67 (8.7)	14 (4.8)	NS
Anti-TNF-α					
No surgery	13/38 (34.2)*	16/95 (16.8)[&]	86/679 (12.7)*	19/259 (7.3)*,[&]	0.05
Plus surgery	0	0	23	4	

E1, ulcerative proctitis; E2, left-sided UC; E3, extensive colitis; FU, follow-up; IQR, interquartile range TNF-α, tumour necrosis factor-α.
[a]Bonferroni corrected differences.
*,[&]Variables causing the difference.

Table 5. Association between age at disease onset, initial disease location and outcome in patients with ulcerative colitis (multivariate cox proportional hazard regression)

	Total colectomy (UC only)			Disease progression (UC only)			Backwash ileitis		
Outcomes	RR	95% CI	*P* value	RR	95% CI	*P* value	RR	95% CI	*P* value
Age category (< 17 years)	0.52	0.10–2.60	0.4	1.91	0.41–8.91	0.41	2.37	0.52–10.85	0.27
Age category (< 40 years)	0.73	0.23–2.40	0.6	0.82	0.20–3.40	0.79	2.19	0.54–8.91	0.28
Age category (>40 years)	0.85	0.29–3.5	0.8	1.28	0.30–5.45	0.47	4.36	1.05–18.05	0.04
Initial location E2	0.54	0.33–0.91	0.02	1.47	1.0–2.15	0.05	0.62	0.45–0.85	0.003
Initial location E1	0.34	0.16–0.71	0.004	1.48	0.93–2.36	0.10	0.53	0.36–0.79	0.002
Ever treated with anti-TNF-α	2.47	1.48–4.11	0.001	1.32	0.83–2.1	0.24	1.94	1.36–2.75	< 0.001

Age category < 10 years and pancolonic initial location are treated as base risk and do not appear.
CI, confidence interval; E1, ulcerative proctitis; E2, left-sided UC; TNF-α, tumour necrosis factor-α; UC, ulcerative colitis.

In summary, in paediatric-onset patients, the higher rates of strictures and PD and the lack of correlation between these factors and the initial location of disease suggest that factors other than the recently reported genetic determinants of either colonic or ileal disease [26], may drive inflammation, thus resulting in a chronic inflammatory course of disease that is more difficult to control.

The comparisons of UC patients by groups categorized according to age at onset yielded the following picture: at baseline, the overall rate of extensive colitis and the rate of chronic architectural changes in the initial biopsy were higher in the paediatric-onset cohort than in the adult-onset cohort, a difference consistent with the reports of other groups [16,27–30]. Still, the rate at which patients with initially left-sided colitis or proctitis were diagnosed with progression or extension of disease was similar in all age groups, and the overall total colectomy rate was low, with no difference observed between age groups as reported previously by other authors [6,7]. In addition, backwash ileitis, previously reported to occur in ~20% of children and adults [29], was observed with the expected rate in adult-onset patients. However, progression or extension of disease occurred more rapidly in patients with at age at disease onset younger than 17 years, whereas backwash ileitis occurred with a lower rate and at greater intervals from diagnosis in paediatric-onset UC and finally, the rate of anti-TNF-α antibody treatments was significantly higher in paediatric-onset patients without colectomy when assessed independent of the initial disease location.

In summary, the fact that the pancolitis is the most frequent initial location in paediatric-onset UC may mask differences in disease behaviour. Only the higher rates of treatment with biologic agents and the shorter interval between diagnosis and disease extension point towards the presence of a more aggressive disease in paediatric UC patients.

The present study has several limitations. First, this study is not population based. In Switzerland, many adult IBD patients are followed by gastroenterologists in private practice, particularly patients with uncomplicated diseases living in regions without easy access to university hospitals. Second, the patient data for disease evolution and treatment choices before study inclusion were not available and the performance of comparisons of these variables between age groups was not possible. Third, data on the pubertal stages of patients with early-onset IBD were not available, and some patients may have been miscategorized according to age because of delayed puberty. Fourth, the disease duration was the longest in patients diagnosed at more than 40 years of age, which was likely one reason why a higher rate of complications was found in this age group. Finally, our paediatric groups were small in size, and the question of whether complications are correlated with genetic predisposition, as seems to be the case in adult-onset disease, should be answered by looking at larger cohorts. Nevertheless, we showed that paediatric-onset IBD was associated with the most significant burden of intestinal complications, and we are the first to present a comparative overview of these complications.

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Conflicts of interest

There are no conflicts of interest.

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